

Molecular Mechanics Modeling of Organic Backbone of Metal-Free and Coordinated Ligands

JOHAN E. BOL,¹ CHRISTIAN BUNING,² PETER COMBA,²
JAN REEDIJK,¹ MARC STRÖHLE²

¹Leiden Institute of Chemistry, Gorlaeus Laboratories, PO Box 9502, NL-2300 RA Leiden, The Netherlands

²Anorganisch-Chemisches Institut, Universität Heidelberg, Im Neuenheimer Feld 270, D-69120 Heidelberg, Germany

Received 14 August 1997; accepted 9 October 1997

ABSTRACT: A new molecular mechanics force field has been developed that takes into account the fact that, upon coordination to a transition metal ion, the redistribution of electron density leads to small but significant structural changes in the organic backbone of the ligand. Structural studies indicate that the perturbation by coordination to a metal ion extends to the α -carbon atom of the donor, the perturbation is roughly independent of the metal center for M^{2+} and M^{3+} and negligible for M^{+} , and the perturbation of the $C_{\alpha}-C_{\alpha'}$ bond is roughly independent of the donor atom. New parameter sets for oxalates, imidazoles, and pyrazoles are also presented. The refined parameters have been validated with a large number of monodentate, multidentate, and macrocyclic ligands. © 1998 John Wiley & Sons, Inc. *J Comput Chem* 19: 512–523, 1998

Keywords: molecular mechanics; force field; transition metal compounds; coordinated ligands; organic backbone

Correspondence to: Prof. P. Comba; e-mail: comba@akcom-ba.oci.uni-heidelberg.de

Contract/grant sponsor: German Science Foundation

Contract/grant sponsor: Fonds of the Chemical Industry

This article includes Supplementary Material available from the authors upon request or via the Internet at <ftp.wiley.com/public/journals/jcc/suppmat/19/512> or <http://journals.wiley.com/jcc/>

Introduction

Coordination of a ligand to a metal ion generally reduces the electron density at the donor atom, and it has been recognized that for coordinated amines, for example, the N—C bond distances increase upon coordination from ca. 1.47 Å in the metal-free ligand to ca. 1.48 Å.¹ This and similar structural effects are rather small, and they are of increasing importance when cumulative effects occur, such as is the case in dinucleating ligands with extended bridges between the coordination sites. So far, force fields used by coordination chemists have usually been fitted to structural data of coordination compounds; therefore, these force fields are not necessarily applicable to purely organic molecules. Indeed, the accuracy of structural predictions produced with these force fields, when used for organic molecules, is significantly lower compared to results from calculations with organic force fields used for organic molecules and compared to the computation of coordinated ligands using coordination chemists' force fields.¹

The neglect of electron delocalization might lead to inaccurate predictions and to misinterpretations when complexation reactions are modeled with the aim of predicting and interpreting complex stabilities and metal ion selectivities, based on the computed hole sizes and structural, as well as thermodynamic, reorganization and preorganization factors.^{1–6} Also, structural predictions involving coordination compounds with extended organic backbones might be unacceptably inaccurate, because the errors are cumulating rather than cancelling; this is specifically true for spacer groups between two or more metal sites. Among others, it is for that reason that the computation of metal–metal distances of dinuclear complexes was often rather poor.^{7–10} We now present a new force field for coordination compounds that may also be used for the optimization of metal-free ligands (i.e., for organic molecules).

Observed Structural Variations

The type of structural data considered is shown in Figure 1, which also describes the nomenclature used in Tables I–III where averaged experimental

structural data are tabulated.^{11–18} Assembled in Table I are donor atom—C_α, C_α—C_β, and C_α—C_{α'} bond distances of metal-free and coordinated amine ligands. It emerges that, upon coordination to a transition metal center, the donor atom—C_α bond is elongated by ca. 1%, whereas the C_α—C_{α'} bond is compressed by ca. 1%. The C_α—C_β bond remains roughly unperturbed.

Structural data of oxalato complexes are listed in Table II. The perturbation of the ligand bond distances upon coordination to a 3+ cation is similar to that of the amine ligands. However, the most striking structural effect here is a significant decrease of the M^{III}—O—C valence angle along the 3d row from 119° for Ti^{III} (close to *sp*²) to 112° for Co^{III} (close to *sp*³). The geometry around the carboxylate carbon atoms is nearly constant and similar to that of the metal-free ligand. It is tempting to attribute the variation of the M^{III}—O—C angle to a decreasing π donation of the carboxylate oxygen along the 3d row (increasing number of electrons in the *t*_{2g} π set of the *d* orbitals of the metal center). Similar effects have been used to interpret structural, thermodynamic, and kinetic data of coordinated EDTA-type ligands.¹⁹ However, from the structural data in Table II it also follows that the decrease of the M^{III}—O—C angle is strongly correlated to the expected compression of the M^{III}—O bond distance from 2.1 to 1.9 Å and a concomitant increase of the bite angle from 74° to 86°. Thus, with the rigidity of oxalate and the observed planarity of the five-membered chelate rings, the variation of the M^{III}—O—C angle may also be interpreted as a structural consequence of the M^{III}—O distances. In the context of the present study it is immaterial whether the geometry around the carboxylate donor atoms is the result of structural effects or due to electronic preferences. An important fact is, however, that the specific geometries are such that the increasing strength of π donation by the carboxylate oxygens is possible for the lighter 3d metal ions.

From the structural data of Cu^{II} compounds with imidazole and pyrazole ligands (Table III) it emerges that the main difference is the Cu—N bond distance, which is similar for the imidazole and benzimidazole complexes and significantly longer for the pyrazole compounds. This is in line with differences in the p*K*_a values of the metal-free ligands. However, the coordination properties of the two types of ligands are rather similar and this

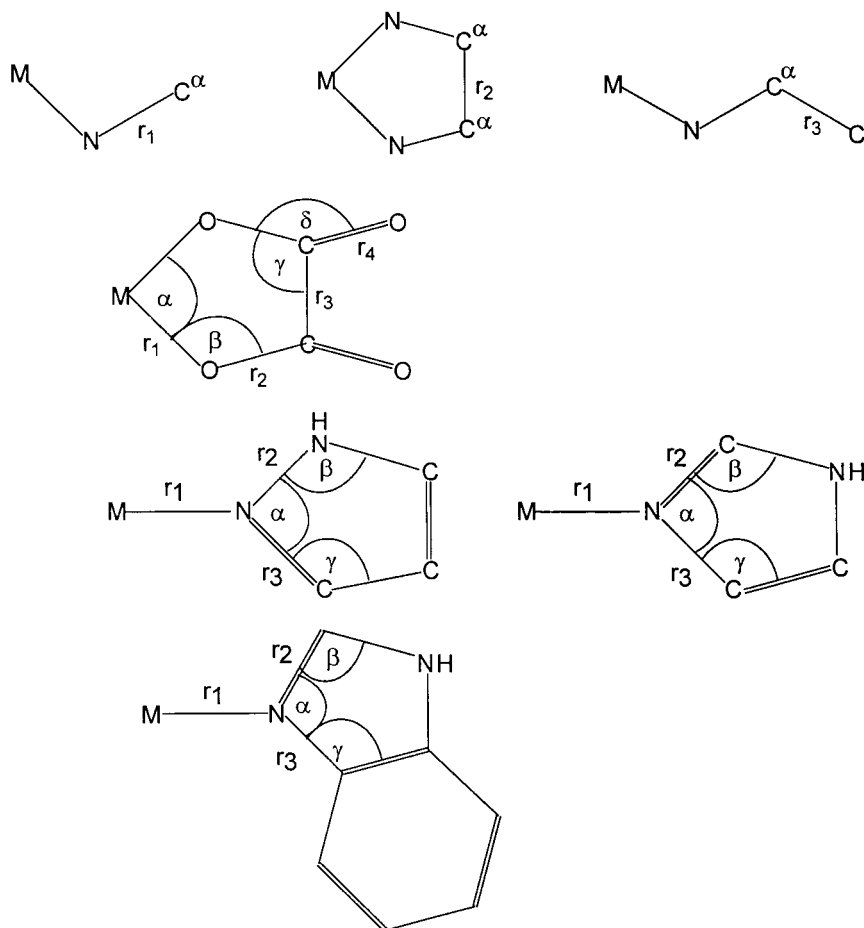


FIGURE 1. The type of structural data considered in this study and the nomenclature used in Tables I–XIV.

emerges also from the close similarity of the ligand field spectra, indicating that both ligand types have similar bonding characteristics. Therefore, the differences in basicity and complex stability might be due to some extent to steric effects. Our parameterization (*vide infra*) indicates that a common parameter set for aromatic five-membered ring nitrogen donors leads to structural predictions of reasonable accuracy.

The approximations used for the force field refinement are based on the structural information discussed above and the desire to keep the parameterization as simple as possible. Strain energy minimized structures were produced with MO-MEC,²⁰ using the set of potential energy functions and a parameterization described previously.^{21,22}

Refined Force Field Parameters and Computed Structures

The experimental structural data of Tables I–III were used to optimize the extended force field. The parameters for the areas of the molecules that are not perturbed by the metal ion are similar but, due to some differences in the set of potential energy functions used in different force fields, not identical to parameter sets that are routinely used for organic compounds.^{23,24} In the course of the refinement of our force field, we also modified the torsional angle parameters for aromatic residues.²¹ These were carefully fitted to a series of structures of metal-free ligands and to their coordination

TABLE I.
Averages of Observed Structural Parameters of Metal-Free and Coordinated Amine Ligands.

	en	cyclam	NH ₂ -Me	NH ₂ -Et	dach	tacn	sar	diammac	Average
L									
<i>r</i> ₁ (Å)	1.46 (0.02 / 6)	—	—	1.46 (0.01 / 2)	1.47 (0.01 / 6)	1.46 (0.01 / 1)	1.46 (0.02 / 2)	—	1.46
<i>r</i> ₂ (Å)	1.49 (0.02 / 6)	—	—	—	1.52 (0.01 / 6)	1.52 (0.01 / 1)	1.51 (0.01 / 2)	—	1.51
<i>r</i> ₃ (Å)	—	—	—	1.48	—	1.52 (0.01 / 2)	— (0.01 / 6)	1.53	1.51 (0.02 / 2)
M^(III)L									
<i>r</i> ₁ (Å)	1.48 (0.02 / 276)	1.48 (0.02 / 34)	1.47 (0.01 / 10)	—	1.49 (0.02 / 33)	1.48 (0.02 / 12)	1.50 (0.04 / 8)	1.48 (0.02 / 18)	1.48
<i>r</i> ₂ (Å)	1.49 (0.04 / 276)	1.49 (0.03 / 34)	—	—	1.51 (0.03 / 33)	1.47 (0.05 / 12)	1.49 (0.03 / 8)	1.48 (0.06 / 18)	1.49
<i>r</i> ₃ (Å)	—	1.52 (0.02 / 34)	—	—	1.52 (0.02 / 33)	—	1.53 (0.03 / 8)	1.53 (0.01 / 18)	1.52
M^(III)L									
<i>r</i> ₁ (Å)	1.47 (0.02 / 102)	1.48 (0.01 / 4)	—	—	1.49 (0.01 / 14)	1.48 (0.03 / 14)	1.47 (0.01 / 2)	1.48 (0.03 / 9)	1.48
<i>r</i> ₂ (Å)	1.48 (0.05 / 102)	1.49 (0.01 / 4)	—	—	1.52 (0.01 / 14)	1.50 (0.03 / 14)	1.48 (0.02 / 2)	1.51 (0.01 / 9)	1.50
<i>r</i> ₃ (Å)	—	1.51 (0.015 / 4)	—	—	1.52 (0.01 / 14)	—	1.51 (0.01 / 2)	1.53 (0.01 / 9)	1.52

The standard deviation and the number of reference structures are given in parentheses.

For the definition of structural parameters see Figure 1.

The reference structures are listed in the Supplementary Material.

en = 1,2-diaminoethane; NH₂-Me = methylamine; NH₂-Et = ethylamine; dach = 1,2-diaminocyclohexane; tacn = 1,4,7-triazacyclononane; sar = 3,6,10,13,16,19-hexaazabicyclo[6.6.6]eicosane; diammac = 6,13-diamino-6,13-dimethyl = 1,4,8,11-tetraazacyclotetradecane; cyclam = 1,4,8,11-tetraazacyclotetradecane; M^(III) = Cr^(III), Mn^(III), Fe^(III), Co^(III). M^(II) = Ni^(II), Cu^(II), Zn^(II). The formula used to determine the standard deviation:

$$SD = \sqrt{\frac{n\sum x^2 - (\sum x)^2}{n^2}}$$

TABLE II.
Observed Structural Parameters of Oxalate and M^{III} Oxalato Complexes.

	<i>r</i> ₁ (Å)	<i>r</i> ₂ (Å)	<i>r</i> ₃ (Å)	<i>r</i> ₄ (Å)	α (°)	β (°)	γ (°)	δ (°)	Plane ^a	Data Set
Ti ³⁺ (ref. 11)	2.1	1.26	1.53	1.22	74.3	118.7	113.5	126.2	0.02 (0.13)	2
V ³⁺ (ref. 12)	2.0	1.27	1.54	1.21	80.3	115.5	114.1	125.8	0.0 (0.07)	2
Cr ³⁺ (ref. 13)	1.97	1.28	1.54	1.22	82.2	114.3	115.6	125.4	0.045 (0.0)	3
Mn ³⁺ (ref. 14)	2.00	1.28	1.56	1.22	80.9	115.6	113.6	126.8	0.05 (0.1)	4
Fe ³⁺ (ref. 15)	2.00	1.28	1.54	1.22	80.4	115.6	114.4	125.8	0.03 (0.16)	1
Co ³⁺ (ref. 16)	1.90	1.29	1.54	1.23	86.37	112.3	114.7	124.2	0.14 (0.07)	6
H ₂ ox (ref. 17)	—	1.29	1.55	1.22	—	—	112.4	127	—	9
ox ²⁻ (ref. 18)	—	1.27	1.56	1.24	—	—	115.6	126.3	—	4

For the definition of structural parameters, see Figure 1. The data given are averages of all relevant distances and angles.

^a RMS deviation from the best plane of C₂O₄²⁻ (Å) (distance of M from that plane, Å).

TABLE III.
Averages of Observed Structural Parameters of Cu^{II} Imidazole, Cu^{II} Benzimidazole, and Cu^{II} Pyrazole Compounds.

	r_1 (Å)	r_2 (Å)	r_3 (Å)	α (°)	β (°)	γ (°)	Data Set
Cu ^{II} imidazole	1.98	1.32	1.38	106	111	109	8
Cu ^{II} benzimidazole	1.98	1.32	1.39	106	112	109	4
Cu ^{II} pyrazole	2.04	1.35	1.33	106	110	110	9

For structural parameters, see Figure 1. For references, see Table VII. The data given are averages of all relevant distances and angles.

compounds, including pyridine, benzene, and paracyclophane groups. All new and refined parameters are given in Table IV. (For the definition of atom types see Fig. 2.) The improved accuracy

of computed structures is demonstrated in Tables V and VI. Due to the differentiation between the part of the ligand backbone that is perturbed by the metal center and the area that is not, there is a

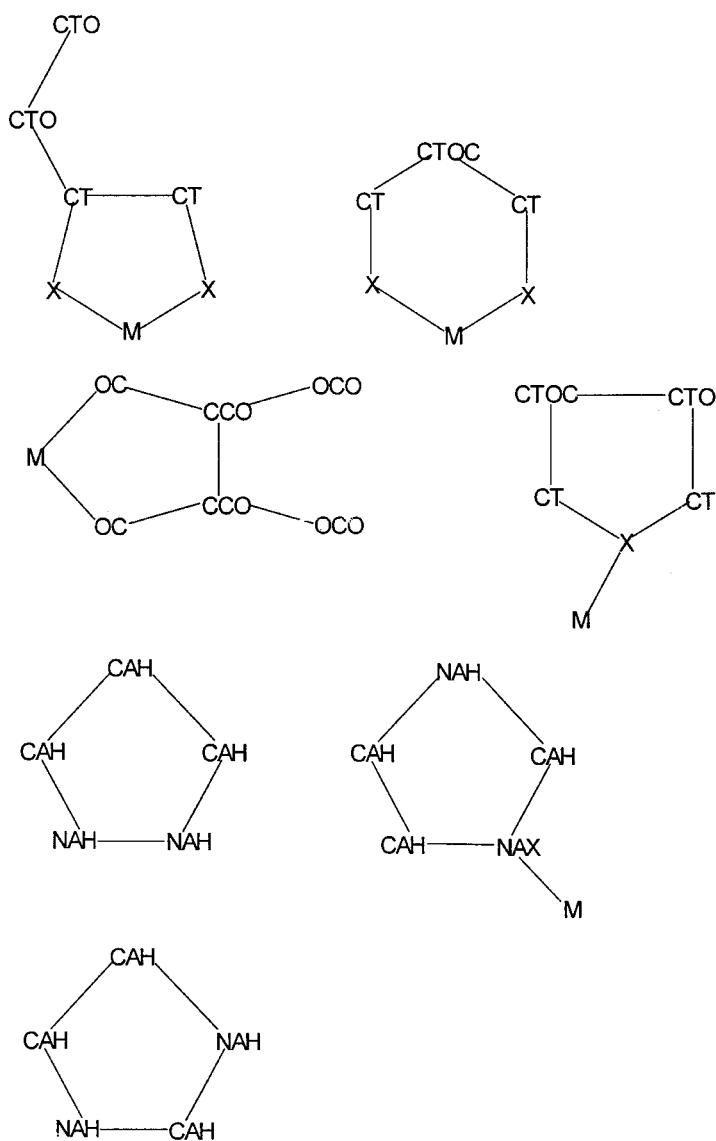


FIGURE 2. Definition of atom types used in Table IV.

TABLE IV.
New MOMECE Force Field Parameters.

Bond Stretch Parameters				Valence Angle Parameters				
Atom 1	Atom 2	k_b (mdyn Å ⁻¹)	r_0 (Å)	Atom 1	Atom 2	Atom 3	k_θ (mdyn Å rad ⁻²)	θ_0 (rad)
CTO	CTO	5.000	1.505	CT	CTO	CTO	0.450	1.920
CT	CTO	5.000	1.500	H	CTO	H	0.320	1.911
CTO	CTOC	5.000	1.510	CAH	CAH	CAH	0.100	1.850
CT	CTOC	5.000	1.500	CAH	CAH	CI	0.650	2.304
CTOC	CTOC	5.000	1.490	CAH	CAH	CT	0.650	2.274
CTOC	CTOC	5.000	1.528	CAH	CAH	H	0.450	2.215
CTOC	NTO	6.000	1.480	CAH	CAH	NAH	0.150	1.955
CAH	CAH	1.500	1.370	CAH	CAH	NAX	0.150	1.955
CAH	CI	4.500	1.450	CI	CAH	NAH	0.650	2.112
CAH	CT	3.000	1.490	CT	CAH	NAH	0.650	2.112
CAH	NAH	1.500	1.340	CT	CAH	NAX	0.650	2.112
CAH	NAX	2.500	1.340	NAH	CAH	H	0.350	2.094
CAH	NI	4.500	1.440	NAH	CAH	NAH	0.150	1.955
CAH	H	5.000	0.970	OC	CCO	OC	0.250	2.094
CT	NAH	3.000	1.450	CAH	CI	NI	0.150	2.094
CU2P	NAH	0.900	1.980	CAH	CI	H	0.450	2.094
CU2P	NAX	0.300	2.300	CA	CT	OW	0.450	1.911
CU2P	OC	0.800	1.900	CAH	CT	CA	0.450	1.911
CU2P	OW	0.800	1.900	CAH	CT	CAH	0.450	1.960
NAH	H	2.500	0.910	CAH	CT	CT	0.450	1.960
NAH	NAH	1.500	1.360	CAH	CT	H	0.360	1.909
NAH	NAX	1.500	1.360	CAH	CT	NT	0.450	1.911
CAH	CA	1.500	1.380	CAH	CT	OP	0.450	1.911
CCO	CCO	5.000	1.525	CAH	CT	OW	0.450	1.911
CR3	OC	0.750	1.935	CT	CT	NAH	0.450	1.911
TI3	OC	0.800	2.080	NAH	CT	H	0.360	1.909
TI3	OW	0.500	2.035	NAH	CT	OW	0.450	1.885
V3	OC	0.500	1.920	CAH	NAH	CAH	0.150	1.842
V3	OW	0.500	1.980	CAH	NAH	CT	0.650	2.243
MN3	OC	0.300	1.950	CAH	NAH	CU2P	0.200	2.147
FE3H	OW	0.500	1.900	CAH	NAH	H	0.350	2.094
FE3H	OC	1.000	1.990	CAH	NAH	NAH	0.200	1.885
				CU2P	NAH	NAH	0.200	2.269
				NAH	NAH	CT	0.650	2.094
				NAH	NAH	H	0.350	2.094
				NAX	NAH	CAH	0.200	1.885
				NAX	NAH	CT	0.650	2.094
				CAH	NAX	CU2P	0.100	2.147
				CAH	NAX	NAH	0.200	1.823
				CU2P	NAX	NAH	0.100	2.304
				CI	NI	CU2P	0.100	2.356
				CT	NI	CU2P	0.200	1.920
				NAH	CAH	CA	1.150	2.292
				CAH	CAH	CA	0.150	2.122
				CAH	CA	CA	0.450	2.024
				CAH	CA	H	0.450	2.122
				CR3	OC	CCO	0.400	1.998
				OC	CCO	CCO	0.800	1.993
				OCO	CCO	CCO	0.950	2.115
				MN3	OC	CCO	0.300	2.028
				V3	OC	CCO	0.500	2.030
				TI3	OC	CCO	0.450	2.062
				FE3H	OC	CCO	0.750	2.030

TABLE IV.
(Continued)

Torsional Angle Parameters					Out of Plane Parameters				
Atom	Atom	k_{ϕ} (mdyn Å)	m	ϕ_{offset} (rad)	Atom 1	Atom 2	Atom 3	Atom 4	k_{oop} (mdyn Å rad ⁻²)
CTO	CTO	0.011	3	0.000	CAH	CAH	CAH	H	2
CTO	CTOC	0.011	3	0.000	CAH	CAH	NAH	CT	2
CTOC	CTOC	0.011	3	0.000	CAH	CAH	NAH	CI	2
CA	CA	0.050	2	0.000	CAH	CAH	NAH	H	2
CA	NP	0.050	2	0.000	CAH	CAH	NAX	CT	2
CCO	CCO	0.000	2	3.097	CAH	NAH	NAH	CI	2
CAH	CAH	0.015	2	1.571	CAH	NAH	NAH	H	2
CAH	CI	0.025	2	1.571	CA	NP	CA	H	2
CAH	CT	0.0005	6	0.524	CA	NP	CT	H	2
CAH	NAH	0.009	2	1.571	CCO	OC	OC	OC	0.5
CAH	NAX	0.0025	2	1.571	CI	NI	CAH	H	1.5
CAH	NI	0.003	2	1.571	OW	CT	CU2P	CU2P	0.5
CT	NAH	0.0005	6	0.524	CAH	NAH	NAH	CT	2
NAH	NAH	0.020	2	1.571	CAH	CAH	CA	NAH	2
NAH	NAX	0.065	2	1.571	CA	CAH	CA	H	2
CAH	CA	0.065	2	1.571					

For atom type labels, see Figure 2. The complete force field with all parameters published so far (and used in the current work) is given as a supplementary table. The structures with oxalate and those with imidazole, benzimidazole, and pyrazole were optimized with a points on a sphere model (“Urey–Bradley” force field²¹); for the other compounds an additional perturbation (*d*-electron effects, harmonic sine function²²) was used. 1 dyn = 10⁻⁵ N.

TABLE V.
Averages of Calculated Free Ligand Structures.

	en	cyclam	NH ₂ —Me	NH ₂ —Et	dach	tacn	sar	diammac	Average
Refined force field									
r_1 (Å)	1.49	1.5	1.49	1.49	1.48	1.50	1.50	1.50	1.495
r_2 (Å)	1.51	1.51	—	—	1.52	1.52	1.52	1.52	1.52
r_3 (Å)	—	1.51	—	1.51	1.51	—	1.52	1.53	1.52
RMS ^a (Å)	0.112	0.156	0.103	0.115	0.328	0.22	0.49	0.467	
Original force field									
r_1 (Å)	1.49	1.50	1.49	1.49	1.49	1.50	1.50	1.50	1.495
r_2 (Å)	1.50	1.51	—	—	1.51	1.51	1.51	1.51	1.51
r_3 (Å)	—	1.51	—	1.50	1.51	—	1.52	1.52	1.51
RMS ^a (Å)	0.115	0.125	0.103	0.116	0.373	0.117	0.957	0.591	
MM +									
r_1 (Å)	1.44	1.45	1.44	1.44	1.44	1.44	1.45	1.45	1.44
r_2 (Å)	1.53	1.54	—	—	1.53	1.54	1.54	1.54	1.54
r_3 (Å)	—	1.54	—	1.53	1.53	—	1.54	1.55	1.54

^a RMS overlay of the MOMECS derived structure and the MM + structure without hydrogens. The formula used to determine the root mean square (RMS) value:

$$\text{RMS} = \sqrt{\frac{\sum_N (x_a - x_b)^2 + (y_a - y_b)^2 + (z_a - z_b)^2}{N}}.$$

TABLE VI.

Comparison Between Observed and Computed Structures Using Original^{19,20} and Refined Force Fields.

	Refined force Field			Original Force Field		
	RMS ^a (Å)	RMS ^{a,b} (Å)	RMS ^{b,c} (Å)	RMS ^a (Å)	RMS ^{a,b} (Å)	RMS ^{b,c} (Å)
[Cr ^(III) (tn) ₃] ³⁺	0.215	0.124	0.098	0.225	0.131	0.103
[Cr ^(III) (diamsar)] ³⁺	0.133	0.070	0.025	0.298	0.153	0.074
[Cr ^(III) (diammac)] ³⁺	0.251	0.135	0.044	0.251	0.136	0.044
[low-spin Fe ^(III) (diammac)] ³⁺	0.144	0.062	0.059	0.144	0.062	0.059
[Co ^(III) ((R)-ala-(S)-ppm)] ²⁺	0.325	0.256	0.045	0.278	0.197	0.060
[Ni ^(II) (diammac)] ²⁺	0.106	0.056	0.042	0.120	0.056	0.046
[mer Ni ^(II) (ditn) ₂] ²⁺	0.269	0.169	0.103	0.270	0.170	0.104
[Ni ^(II) (tach) ₂] ²⁺	0.046	0.024	0.029	0.046	0.025	0.029
[Cu ^(II) ([15]aneS ₄)(H ₂ O) ₂] ²⁺	0.178	0.143	0.121	0.178	0.143	0.121
[Cu ^(II) ([16]aneS ₄)(H ₂ O) ₂] ²⁺	0.080	0.050	0.036	0.080	0.050	0.036
[Cu ^(II) (3,7-diazanonan-1,9-diamine)(H ₂ O) ₂] ²⁺	0.090	0.053	0.045	0.090	0.053	0.045
[Cu ^(II) (mn[14]aneN ₄)(H ₂ O) ₂] ²⁺	0.151	0.108	0.020	0.152	0.108	0.020
[Cu ^(II) (mn[14]aneN ₂ S ₂)(H ₂ O) ₂] ²⁺	0.247	0.197	0.031	0.246	0.198	0.031
[Cu ^(II) (mn[15]aneN ₄)(H ₂ O) ₂] ²⁺	0.283	0.233	0.111	0.250	0.180	0.131
[Cu ^(II) (mn[16]aneN ₄)(H ₂ O) ₂] ²⁺	0.191	0.151	0.052	0.211	0.161	0.080
[Zn ^(II) (diammac)] ²⁺	0.130	0.074	0.062	0.130	0.074	0.062
Average	0.177	0.119	0.058	0.186	0.119	0.065

^a See footnote a in Table V.^b RMS without H atoms.^c RMS of the chromophores (metal ion and donor atoms).

tn = 1,3-diaminopropane; diamsar = 3,6,10,13,16,19-hexaazabicyclo[6.6.6]eicosane-1,8-diamine; diammac = 6,13-diamino-6,13-dimethyl-1,4,8,11-tetraazacyclotetradecane; ala = alanine; ppm = *N,N*-bis(2-pyrrolidinylmethyl)propane-1,3-diamine; ditn = bis(3-aminopropyl)amine; tach = *cis,cis*-cyclohexane-1,3,5-diamine; [15]aneS₄ = 1,4,8,12-tetrathiacyclopentadecane; [16]aneS₄ = 1,5,9,13-tetrathiacyclohexadecane; mn[14]aneN₄ = 6,13-dimethyl-6,13-dinitro-1,4,8,11-tetraazacyclotetradecane; mn[14]aneN₂S₂ = 6,13-dimethyl-6,13-dinitro-1,4-dithia-8,11-diazacyclotetradecane; mn[15]aneN₄ = 6,13-dimethyl-6,13-dinitro-1,4,8,11-tetraazacyclotetradecane; mn[16]aneN₄ = 6,13-dimethyl-6,13-dinitro-1,5,9,13-tetraazacyclohexadecane.

small but significant improvement of the accuracy of the computed structures of the coordination compounds. The refined force field is now well suited for the optimization of structures of the metal-free ligands (i.e., of organic molecules).

Recently we quantitatively analyzed the influence of alkyl substitution on the nucleophilicity of aliphatic amine ligands.²⁵ It was concluded that ammonia and primary, secondary, and tertiary amines should have different metal-amine force field parameter sets. However, based on the structural analysis a further increase of the complexity of the parameterization was thought to not be warranted.⁷ This follows also from the present structural analysis (see Table VI).

The new parameterization schemes developed in this study include metal complexes with oxalate, imidazole, benzimidazole, and pyrazole also ligands. The quality of the computed structures of

these compounds is presented in Table VII.^{26–64} There is an important difference between five- and six-membered (aromatic) ring systems in terms of molecular mechanics modeling. While for six-membered rings there are 1,4-nonbonded (van der Waals) interactions between the ring atoms, there are none in five-membered rings. This has consequences for the bond stretching parameters and the parameterization of the torsional angles and the out of plane potential. Because in the presently used parameterization scheme any repulsion force within the ring is missing in five-membered heterocycles, there is a naively unexpectedly large difference of force constants and strain free distances between five- and six-membered rings. Also, the planarity and intraring valence angles require different approaches for the two types of rings. Obviously, the differences in bond stretching parameters are not related to differences in the corre-

TABLE VII.
Comparison of Observed and Computed Structures of Oxalato and Cu^{II} Imidazole, Pyrazole, and Benzimidazole Compounds.

	RMS ^a
Ti(H ₂ O) ₃ (ox) ₂ ⁻ (ref. 26)	0.449
Ti(H ₂ O)(ox) ₃ ⁻ (ref. 27)	0.250
V(H ₂ O) ₂ (ox) ₂ ⁻ (ref. 28)	0.030
V(H ₂ O) ₂ (ox) ₂ ⁻ (ref. 28)	0.030
K ₃ Cr(ox) ₃ (ref. 29)	0.197
(NH ₄) ₃ Cr(ox) ₃ (ref. 30)	0.154
Rb ₃ Cr(ox) ₃ (ref. 31)	0.174
(C(NH ₂) ₃) ₃ (Cr(ox) ₃) (ref. 32)	0.409
Na ₃ Cr(ox) ₃ (ref. 33)	0.146
(NH ₄) ₃ Cr(ox) ₃ (ref. 34)	0.187
[Cr(ox)(en) ₂] ⁺ (ref. 35)	0.321
KCr(en)(ox) ₂ (ref. 36)	0.266
[Cr(1,4,8,11-tetraazaundecane)(ox)] ⁺ (ref. 37)	0.150
[Cr(1,5,8,12-tetraazaundecane)(ox)] ⁺ (ref. 38)	0.182
Mn(ox) ₃ ³⁻ (ref. 39)	0.211
Fe(ox) ₃ ³⁻ (ref. 40)	0.060
Fe(ox) ₃ ³⁻ (ref. 41)	0.200
[Cu(ox) ₂] ²⁻ (ref. 42)	0.099
Cu(H ₂ O)(ox)(<i>N</i> -methylpropane-1,3-diamine) (ref. 43)	0.563
[Cu(ox) ₂] ²⁻ (ref. 44)	0.030
[Cu(ox) ₂] ²⁻ (ref. 45)	0.05
Cu(diethylentriamine)(ox) (ref. 46)	0.498
[Co(ox)(en) ₂] ⁺ (ref. 47)	0.211
[Co(ox)(en) ₂] ⁺ (ref. 48)	0.097
[Co(tn) ₂ (ox)] ⁺ (ref. 49)	0.28
Co(diaminopentane) ₂ (ox) ⁺ (ref. 50)	0.148
[Co(1,7-bis(pyrrolidyl)-2,6-diazaheptane)(ox)] ⁺ (ref. 51)	0.450

^aSee footnote a in Table V.

sponding bond strengths. This is just another excellent example^{1,7} to stress the fact that force field parameters are highly interdependent (i.e., the refinement of new parameters strongly depends on the existing parameter field) and force field parameters are not necessarily strongly related to accepted physical principles.

It is common practice to neglect the torsional barrier around metal–ligand bonds.¹ This approach has been justified for the rotation of ammonia in [Co(NH₃)₆]³⁺ where experimental data indicate that there is rapid rotation around the Co–N axis, even at low temperature.⁶⁴ In cases, where π bonding between the metal and the donor occurs, such as in some of the systems modeled in the present study, this certainly is not a realistic approach because the π bonds will confer some directionality on the preferred ligand orientation.

However, the structures studied here do not allow to attribute a specific rotational barrier, and the rigidity of the ligand backbones ensures the observed torsional angles involving the metal centers (see also the comment on π bonding involving oxalate ligands).

Conclusions

Based on the data presented here, we conclude that the refined force field leads to more accurate and more reliable optimized structures of ligands and their coordination compounds. Recent examples indicate that the present force field is also of considerable importance for dinuclear compounds with extended bridges that are not perturbed by

TABLE VII.
(Continued)

	RMS ^a	Cu–Cu Distance (Å)
Cu(Nhdp) ²⁺ (ref. 52)	0.610	3.29
Cu(IP-EA) ²⁺	0.445	4.06
Cu ₂ (3PFM) ₄ ⁴⁺	0.704	4.07
Cu ₂ (BAP-HYPA) ⁴⁺	0.503	3.46
Cu ₂ (BAPEA) ⁴⁺ (ref. 53)	0.460	7.45
Cu ₂ (BAPEA) ⁴⁺ (ref. 53)	0.313	7.24
Cu ₂ (ETPY24PZ) ⁴⁺ (ref. 54)	0.633	6.81
Cu(Htidah) ²⁺ (ref. 55)	0.777	4.35
Cu ₂ (bipyp) ₂ ⁴⁺ (ref. 56)	0.224	3.30
Cu ₂ (biib) ₂ ⁴⁺ (ref. 57)	0.299	3.45
Cu(biib) ²⁺ (ref. 57)	0.310	3.34
Cu(ddaH) ²⁺ (ref. 48)	0.509	
Cu(dbz) ²⁺ (ref. 59)	0.255	
Cu(bimam) ²⁺ (ref. 60)	0.609	
Cu ₂ (ETPY42PZ) ⁴⁺ (ref. 54)	1.476	
Cu(bimam) ²⁺ (ref. 60)	0.967	
Cu(bimam) ²⁺ (ref. 60)	0.383	
Cu ₂ (mtbz) ⁴⁺ (ref. 61)	0.974	2.99
Cu(tbz) ²⁺ (ref. 62)	0.357	
Cu(tbz) ₂ ²⁺ (ref. 62)	0.879	
Cu(mtbz) ²⁺ (ref. 61)	0.415	
Cu(bimam) ₂ ²⁺ (ref. 60)	0.366	
Cu ₂ (biib) ⁴⁺ (ref. 57)	0.629	
Cu(NHed) ₂ ²⁺ (ref. 61)	0.727	
Cu(NHed) ₂ ²⁺ (ref. 61)	0.531	3.10
Cu(tbz) ₂ ²⁺ (ref. 62)	0.797	3.02
Cu(tbz) ₂ ²⁺ (ref. 62)	0.620	
Cu(qbz) ²⁺	1.381	
Cu ₂ (Hbidph) ⁴⁺ (ref. 63)	0.726	5.75

^a RMS without H atoms. See Table V.^b RMS of the chromophores (metal ion and donor atoms). Nhdp = *N*-hydroxy-(3,5-dimethyl)pyrazole; IP-EA = 1-amino-2-(3'-imino-5'-methyl-1'-pyrazolyl)ethane; 3PFM = (3-methylpyrazolyl)-phenylmethanol; BAP-HYPA = 1,3-di(3'-imino-5'-methyl-1'-pyrazolyl)-2-hydroxypropane; BAPEA = (6,17,23,34-tetramethyl)-1,5,10,13,18,22,27,30,35,36,37,38-dodecaaza-pentacyclo-[30.2.1.1^{5,8}.1^{15,18}.1^{22,25}]-octatricontane-6,8(36),15(37),16,23,25(38),32(35),33-octaene; ETPY24PZ = (10,24-di(pyridin-2-ylethyl)-1,5,10,15,19,24,29,30,31,32-decaaza-6,14,20,28-tetramethyl)-pentacyclo-[24.2.1.1^{5,8}.1^{12,15}.1^{19,22}]-dotriaconta-6,8(30),12(31),13,20,22(32),26(29),27-octaene; Htidah = 1,1,6,6-tetrakis-(imidazol-2-yl)-2,5-diazaheptane; bipyp = bis(1,1-imidazol-2-yl)(3-pyridine-2-yl)-2-aza-propane; biib = bis(1,1-imidazol-2-yl)(4-(pyrazol-1-yl)-2-aza-butane; ddaH = bis(2-(3,5-dimethylpyrazol-1-yl)ethyl)amine; dbz = bis(2-benzimidazolyl)ethane; bimam = bis(imidazol-2-yl)methylaminomethane; mtbz = bis(1-methyl-2-benzimidazolyl)propane; tbz = bis(2-benzimidazolyl)propane; NHed = 2-(3,5-dimethylpyrazol-1-yl)ethanol; qbz = bis(2-benzimidazolyl)butane; Hbidph = bis(1,1-imidazol-2-yl)(7-(3,5-dimethylpyrazol-1-yl)-2-aza-5-thia-heptane).

the metal centers.^{7–10} With force fields that are only based on experimental structural data of coordination compounds, the accurate computation of structures of metal-free ligands has not been warranted. This was a considerable problem in studies where molecular mechanics calculations are used to predict and interpret complex stabilities and metal ion selectivities.^{1–6} In particular, in some of the methods used for a quantitative analysis of the ligand preorganization, the strain energy difference between the metal-free and the coordi-

nated ligand, and therefore the structure and strain of the metal-free ligand, are important variables.

Acknowledgments

Generous financial support by the German Science Foundation (DFG) and the Fonds of the Chemical Industry (FCI) is gratefully acknowledged.

References

1. P. Comba and T. W. Hambley, *Molecular Modeling of Inorganic Compounds*, VCH, Weinheim, Germany, 1995.
2. R. D. Hancock, *Prog. Inorg. Chem.*, **28**, 187 (1989).
3. R. D. Hancock, In *Perspectives in Coordination Chemistry*, A. F. Williams, C. Floriani, and A. E. Merbach, Eds., Verlag HCA, Basel, Switzerland, and VCH, Weinheim, Germany, 1992, p. 129.
4. R. D. Hancock, *Acc. Chem. Res.*, **23**, 253 (1990).
5. D. H. Busch, *Acc. Chem. Res.*, **11**, 392 (1978).
6. (a) P. Comba, A. Fath, A. Kühner, and B. Nuber, *J. Chem. Soc., Dalton Trans.*, 1889 (1997); (b) P. Comba, W. Goll, B. Nuber, and K. Várnagy, to appear; (c) P. Comba, K. Gloe, K. Inoue, T. Krueger, H. Stephan, and K. Yoshizuka, to appear.
7. P. Comba, In *Fundamental Principles of Molecular Modeling*, A. Amann, J. C. A. Boeyens, and W. Gans, Eds., Plenum Press, New York, 1996, p. 167.
8. P. V. Bernhardt, P. Comba, T. W. Hambley, S. S. Massoud, and S. Stebler, *Inorg. Chem.*, **31**, 2644 (1992).
9. P. Comba and P. Hilfenhaus, *J. Chem. Soc., Dalton Trans.*, 3269 (1995).
10. P. Comba, T. W. Hambley, P. Hilfenhaus, and D.T. Richens, *J. Chem. Soc., Dalton Trans.*, 533 (1996).
11. (a) D. J. Eve and M. L. Niven, *Inorg. Chim. Acta*, **174**, 205 (1990); (b) M. G. B. Drew and D. J. Eve, *Acta Crystallogr. B*, **33**, 2919 (1977).
12. I. E. Grey, I. C. Madson, K. Sirat, and P. W. Smith, *Acta Crystallogr. C*, **41**, 681 (1985).
13. (a) J. N. van Niekerk and F. R. L. Schoening, *Acta Crystallogr. B*, **5**, 499 (1952); (b) H. Ohbo, H. Okazaki, K. Miyosji, and H. Yoneda, *Bull. Chem. Soc. Jpn.*, **56** 1982 (1983); (c) J. W. Lethbridge, L. S. D. Glasser, and H. F. W. Taylor, *J. Chem. Soc. A*, 1862 (1970); (d) D. Taylor, *Aust. J. Chem.*, **31**, 1455 (1978); (e) E. H. Merrachi, B. F. Mentzen, and F. Chassagneux, *Rev. Chim. Miner.*, **23**, 329 (1986); (f) E. H. Merrachi, B. F. Mentzen, and F. Chassagneux, *Rev. Chim. Miner.*, **24**, 427 (1987).
14. T. Lis and J. Matuszewski, *Acta Crystallogr. Sect. B*, **36**, 1938 (1980).
15. (a) E. H. Merrachi, B. F. Mentzen, F. Chassagneux, and J. Bouix, *Rev. Chem. Miner.*, **24**, 56 (1987); (b) I. Malfant, I. Morgenstern-Badaran, M. Philoche-Levisalles, and F. Lloret, *J. Chem. Soc., Chem. Commun.*, 1338 (1990); (c) J. P. Declercq, J. Fenau-Dupont, and J. Ladriere, *Polyhedron*, **12**, 1031 (1993).
16. (a) M. C. Couldwell, D. A. House, and B. R. Penfold, *Inorg. Chim. Acta*, **13**, 61 (1975); (b) H. Okazaki, Y. Kushi, and H. Yoneda, *J. Am. Chem. Soc.*, **107**, 4183 (1985).
17. Y. Wang, C. J. Tsai, W. L. Liu, and L. D. Calvert, *Acta Crystallogr. Sect. B*, **41**, 131 (1985).
18. D. A. Reed and M. M. Olmstead, *Acta Crystallogr. Sec. B*, **7**, 938 (1981).
19. R. Meier, M. Boddin, S. Mitzenheim, and K. Kanamori, *Metal Ions Biol. Syst.*, **31**, 45 (1996).
20. P. Comba, T. W. Hambley, G. Lauer, and N. Okon, *MO-MEC, A Molecular Modeling Package for Inorganic Compounds*, Lauer & Okon, Heidelberg, Germany, 1997; e-mail: CVS-HD@T-ONLINE.DE.
21. P. V. Bernhardt and P. Comba, *Inorg. Chem.*, **31**, 2638 (1992).
22. P. Comba, T. W. Hambley, and M. Ströhle, *Helv. Chim. Acta*, **61**, 2042 (1995).
23. J.-H. Lii and N. L. Allinger, *J. Am. Chem. Soc.*, **111**, 8576 (1989).
24. S. J. Weiner, P. A. Kollman, D. A. Case, U. C. Singh, C. Ghio, G. Alagona, and S. Proteta, Jr., *J. Am. Chem. Soc.*, **106**, 765 (1984).
25. P. V. Bernhardt and P. Comba, *Inorg. Chem.*, **32**, 2798 (1993).
26. D. J. Eve and M. L. Niven, *Inorg. Chim. Acta*, **205**, 174 (1990).
27. M. G. B. Drew and D. J. Eve, *Acta Crystallogr., B*, **33**, 2919 (1977).
28. I. E. Grey, I. C. Madson, K. Sirat, and P. W. Smith, *Acta Crystallogr., C*, **41**, 681 (1985).
29. D. Taylor, *Austr. J. Chem.*, **31**, 1455 (1978).
30. E. H. Merrachi, B. F. Mentzen, and F. Chassagneux, *Rev. Chem. Miner.*, **23**, 329 (1986).
31. E. H. Merrachi, B. F. Mentzen, and F. Chassagneux, *Rev. Chem. Miner.*, **24**, 427 (1987).
32. L. Golic and N. Bulc, *Acta Crystallogr., C*, **44**, 2065 (1988).
33. N. Bulc, L. Golic, and J. Siftar, *Vestn. Slov. Kem. Drus.*, **29**, 211 (1982).
34. J. N. van Niekerk and F. R. L. Schoening, *Acta Crystallogr.*, **5**, 499 (1952).
35. J. W. Lethbridge, L. S. D. Glasser, and H. F. W. Taylor, *J. Chem. Soc. A*, 1862 (1970).
36. L. S. D. Glasser and J. W. Lethbridge, *J. Chem. Soc., Dalton Trans.*, 2065 (1976).
37. G. A. Kukina, M. A. Poraikoshits, Y. N. Shevchenko, and V. N. Shchurkina, *Koord. Khim.*, **16**, 784 (1990).
38. G. A. Kukina, M. A. Poraikoshits, Y. N. Shevchenko, and V. N. Shchurkina, *Koord. Khim.*, **16**, 189 (1990).
39. T. Lis and J. Matuszewski, *Acta Crystallogr. Sect. B*, **36**, 1938 (1980).
40. E. H. Merrachi, B. F. Mentzen, and F. Chassagneux, *Rev. Chim. Miner.*, **24**, 427 (1987).
41. J. P. Declercq, J. Fenau-Dupont, and J. Ladriere, *Polyhedron*, **12**, 1031 (1993).
42. D. R. Bloomquist, J. J. Hansen, C. P. Landee, R. D. Willett, and R. Buder, *Inorg. Chem.*, **20**, 3308 (1981).
43. A. Pajunen, *Cryst. Struct. Commun.*, **10**, 957 (1981).
44. D. R. Bloomquist, J. J. Hansen, C. P. Landee, R. D. Willett, and R. Buder, *Inorg. Chem.*, **20**, 3308 (1981).
45. U. Geiser, B. L. Ramakrishna, R. D. Willett, F. B. Hulsberger, and J. Reedijk, *Inorg. Chem.*, **26**, 3750 (1987).
46. F. S. Stephens, *J. Chem. Soc. A*, 2493 (1969).
47. D. J. Radanovic, S. R. Trifunovic, S. A. Gruijic, C. Maricondi, M. Parvez, and B. E. Douglas, *Inorg. Chim. Acta*, **33**, 157 (1989).
48. I. Bernal, J. Cetrullo, J. Myrczek, and S. S. Massoud, *J. Coord. Chem.*, **29**, 30 (1993).
49. I. Bernal, J. Cetrullo, J. Myrczek, and S. S. Massoud, *J. Coord. Chem.*, **29**, 287 (1993).
50. R. G. Ball, R. T. Thurier, and N. C. Payne, *Inorg. Chim. Acta*, **30**, 227 (1978).

51. W. A. Freeman, *Inorg. Chem.*, **17**, 2982 (1978).
52. J. E. Bol, H. de Jager, B. Maase, R. A. de Graaf, W. L. Driessen, H. Kooijman, A. L. Spek, and J. Reedijk, unpublished manuscript.
53. J. E. Bol, W. L. Driessen, and J. Reedijk, *J. Chem. Soc., Chem. Commun.*, 1365 (1995).
54. J. E. Bol, B. Maase, G. Gonesh, W. L. Driessen, K. Goubitz, and J. Reedijk, unpublished manuscript.
55. G. J. A. A. Koolhaas, W. L. Driessen, P. J. van Koningsbruggen, J. Reedijk, and A. L. Spek, *J. Chem. Soc., Dalton Trans.*, 3803 (1993).
56. G. J. A. A. Koolhaas, Ph.D. thesis, Leiden University, 1996.
57. G. J. A. A. Koolhaas, W. L. Driessen, J. Reedijk, H. Kooyman, and A. L. Spek, *J. Chem. Soc., Chem. Commun.*, 517 (1995).
58. P. M. van Berkel, W. L. Driessen, R. Hämäläinen, U. Turpeinen, and J. Reedijk, *Inorg. Chem.*, **33**, 5920 (1994).
59. G. A. van Albada, W. J. J. Smeets, N. Veldman, A. L. Spek, and J. Reedijk, *J. Chem. Soc., Dalton Trans.*, unpublished manuscript.
60. G. Mendoza-Diaz, G. J. A. A. Koolhaas, W. L. Driessen, and J. Reedijk, *Acta Crystallogr. Sect. C*, **51**, 918 (1995).
61. G. A. van Albada, W. J. J. Smeets, A. L. Spek, and J. Reedijk, *Inorg. Chem. Acta*, to appear.
62. G. A. van Albada, M. T. Lakin, N. Veldman, A. L. Spek, and J. Reedijk, *Inorg. Chem.*, **34**, 4910 (1995).
63. J. E. Bol, H. de Jager, B. Maase, R. A. de Graaf, W. L. Driessen, H. Kooijman, A. L. Spek, and J. Reedijk, unpublished manuscript.
64. P. H. Kim, *J. Phys. Soc. Jpn.*, **15**, 445 (1960).